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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,767	08/24/2001	William E. Klunk	076333-0281	8947

22428 7590 05/28/2003

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER

JONES, DAMERON LEVEST

ART UNIT	PAPER NUMBER
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1616

DATE MAILED: 05/28/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/935,767

Applicant(s)

KLUNK ET AL.

Examiner

D. L. Jones

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 March 2003 and 27 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 78-130 is/are pending in the application.
- 4a) Of the above claim(s) 78-80, 82, 83, 85-105, 107-110, 112, 115, 116 and 125-130 is/are withdrawn from consideration.

- 5) ☒ Claim(s) 84, 106, 111 and 113 is/are allowed.
- 6) ☒ Claim(s) 81 and 117-123 is/are rejected.
- 7) ☒ Claim(s) 114 and 124 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>15</u> |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

U.S. Patent and Trademark Office
PTO-326 (Rev. 04-01)

Office Action Summary

Part of Paper No. 14

WITHDRAWAL OF PREVIOUS OFFICE ACTION

1. The previous office action is WITHDRAWN in view of the action set forth below.

Note: The previous office action is being withdrawn because an incorrect time period was set for Applicant to reply to the action.

ACKNOWLEDGMENTS

2. The Examiner acknowledges receipt of Paper No. 13, filed 3/5/03, wherein claims 44-77 were canceled and claim 90 was amended.

Note: Claims 78-130 are pending.

RESPONSE TO APPLICANT'S ARGUMENTS/AMENDMENT

3. Applicant's arguments with respect to claims 81 and 117 have been considered but are moot in view of the new ground(s) of rejection.

CLARIFICATION OF RECORD

4. It is duly noted in Applicant's response filed 3/5/03, Paper No. 13, the original claims were restricted into groups and Applicant was respectfully requested to elect a species for search purpose from within the elected group. It is also noted that all of the originally filed claims have been deleted. In particular, in Applicant's response, it is stated that the non-elected species found in the prior art is one which is disclosed by Applicant and Applicant is entitled to a reasonable number of disclosed species in addition to the elected species provide all the claims to each additional species are

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written in dependent form or otherwise include the limitation of an allowed generic claim. Applicant refers to both MPEP 803.02 and 809.02(c) for support. Hence, Applicant's position is that the Examiner improperly rejected the claims since the Examiner considered the elected species and then chose a species enumerated from nowhere in the specification or claims. Instead the Examiner selected from among various substitutents recited in Applicant's genus. Furthermore, Applicant asserts that the Examiner has withdrawn claims directed to non-elected species and requests that the search be expanded to encompass the radiolabeled derivatives of claim 90 that, in Applicant's opinion, would not constitute undue burden on the Examiner.

First, Applicant is reminded that the claims are directed to species that are not enumerated anywhere in the disclosure. Thus, in expanding the search from the elected species to another species, the Examiner may expand the search to any species encompassed by the claims.

In MPEP 803.02, it is disclosed that should no prior art be found that anticipates or renders obvious the elected species, then the search of the Markush type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush type claim with respect to a non-elected species, the Markush type claim shall be rejected and the claims to the non-elected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all non-elected species. Thus, since prior art was found to render obvious the species of the expanded search, the Examiner is not required to search each and every species encompassed by the formula of Structure D. If prior art were not found while

searching, the Examiner would have continued to search until Applicant was given a reasonable number of allowable species. However, in this instance, prior art has been found.

In regards to the Examiner searching both radiolabeled and non-radiolabeled compounds, Applicant's request is denied because a separate search and consideration is necessary to determine if the prior art would anticipate or render obvious the compounds. For example, prior art rendering anticipating a non-radiolabeled compound would not necessarily anticipate or render obvious the radiolabeled compound because the reference would need to provide motivation to add a radiolabel to a compound known in the art without a label. Furthermore, the radiolabeled and non-radiolabel compounds would classify differently. Also, it should be noted that a burdensome search is necessary since normally, compounds used for certain types of imaging techniques require the presence of a chelating agent and metal. Thus, further supporting the fact that a non-labeled compound may not render obvious a label compound that requires the attachment of a chelating agent in order to be radiolabeled.

Note: Initially, Applicant's elected species was searched and found to be allowable over the prior art of record. Thus, the search was expanded to **EXP #1** (Z = S; Y = NR₁R₂; R₁ – R₇ = H; R₈ = CH₃; R₉ = H; and R₁₀ = H). The search was not further expanded because prior art was found which could be used to reject the claims.

WITHDRAWN CLAIMS

5. Claims 78-80, 82, 83, 85-105, 107-110, 112, 115, 116, and 125-130 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention/species.

NEW GROUNDS OF REJECTIONS

103 Rejections

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 81 and 117-123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vitek et al (US Patent No. 5,935,927).

Vitek et al disclose compositions and methods for stimulating amyloid removal in amyloidogenic diseases using advanced glycosylation endproducts (see entire document, especially, abstract). In particular, Vitek et al disclose the use of 2-(4-aminophenyl)-6-methyl benzothiazole in combination with bis(trichloromethyl) carbonate and xylene in generating an advanced glycosylating endproduct (AGE)-modified thioflavin (column 32, Example 3). The structure of 2-(4-aminophenyl)-6-methyl benzothiazole is encompassed in the instant invention when Z = S; Y = NR₁R₂; R₁ – R₇ = H; R₉ and R₁₀ = H; and R₈ = CH₃ (this species will be referred to as **EXP #1**). In

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addition, Vitek et al disclose that involvement of AGE receptor mediated uptake by phagocytic cells may be evaluated with a standard binding assay. The assay may be performed wherein the content of the label in the cell fraction and culture fluid fraction is measured by TCA precipitation of the labeled compounds. Also, the wells may be precoated with the labeled test and control compounds in their soluble or insoluble aggregated forms, incubated with cells, and the presence of labeled compounds in the cell culture fluid assayed. 125-Iodine is a possible label for the compounds (columns 22-23, bridging paragraph; column 23, lines 15-30). The AGE compounds may be prepared and are capable of use in connection with various diagnostic techniques including immunoassays such as a radioimmunoassay using for example, a receptor or other ligand to and AGE that may either be unlabeled or labeled. The AGE compounds may optionally labeled with an enzyme, a compound that fluoresces and/or a radioactive element, and later introduced into a tissue or fluid sample of a mammal. After the labeled material or its binding partner(s) has had an opportunity to react, the resulting mass may be examined by known techniques which may vary with the nature of the labeled attached. Some commonly employed techniques include radioactive elements, enzymes, and chemicals that fluoresce when exposed to ultraviolet light. Suitable radioactive elements for use with the compounds include 3H, 14C, 32P, 35S and 59Fe among others. If a radioactive element is used, a currently available counting procedure may be used. In the instant wherein the label is an enzyme, detection may be accomplished by any of the presently utilized colorimetric, spectrophotometric, fluorospectrophotometric, thermometric, amperometric, or gasometric techniques

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(column 25, lines 30-61). While Vitek et al do not disclose a compound wherein R8 = H or ethyl, propyl, or butyl, the reference does disclose a compound wherein R8 = methyl. Also, it is noted that Vitek et al do not list all the possible techniques wherein their compounds may be utilized.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the methyl group of Vitek et al with a hydrogen as set forth in Applicant's claim because it is well established that the substitution of methyl for hydrogen (and vice versa) on a known compound is not a patentable modification absent unexpected or unobvious results (In re Wood, 582 F.2d 638, 199 USPQ 137 (CCPA 1978)).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace R8 = methyl with ethyl, propyl, or butyl because a skilled practitioner in the art would recognize that a homologous series is a family of chemically related compounds that vary from member to member by a CH₂ group. Thus, since the characteristics normally possessed by members of a homologous series are principally the same, varying gradually from member to member, chemists knowing the properties of one member of a series would in general know what to expect in adjacent members so that a mere difference in degree is not the marked superiority which will ordinarily remove the unpatentability of adjacent homologues of old substances.

ALLOWABLE CLAIMS

8. Claims 84, 106, 111, and 113 are allowable over the prior art of record. In particular, the claims are allowable over the prior art of record for the elected species only. Specifically, the claims are allowable wherein the species is that of Structure D wherein $Z = S$; $Y = NR_1R_2$; $R_1 = H$; $R_2 = CH_3$; $R_3-R_7 = H$; $R_8 = OR'$ wherein $R' = H$; $R_9 = H$; and $R_{10} = H$. The elected species is distinguished over the prior art of record because the prior art neither anticipates nor renders obvious the specific species claimed by Applicant.

OBJECTED CLAIMS

9. Claims 114 and 124 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Note: Both claims 114 and 124 in combination with the limitations of their respective independent and intervening claims are allowable over the prior art of record for the elected and expanded species (EXP #1) only.

Elected Species: $Z = S$; $Y = NR_1R_2$; $R_1 = H$; $R_2 = CH_3$; $R_3-R_7 = H$; $R_8 = OR'$ wherein $R' = H$; $R_9 = H$; and $R_{10} = H$; and

EXP #1: $Z = S$; $Y = NR_1R_2$; $R_1 - R_7 = H$; $R_8 = CH_3$; $R_9 = H$; and $R_{10} = H$.

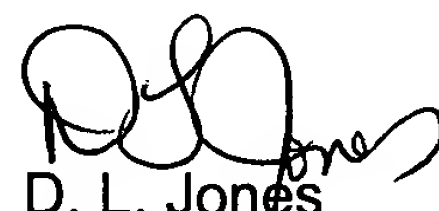
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (703) 308-4640.

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The examiner can normally be reached on Mon.-Fri. (alternate Mon.), 6:45 a.m. - 4:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose' Dees can be reached on (703) 308- 4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.


D. L. Jones
Primary Examiner
Art Unit 1616

May 28, 2003